

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-21 (cancelled)

Claim 22 (withdrawn-currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of ~~comprises~~:

(a) [[a]] an ethyleneoxide containing chemically defined valency platform molecule comprising a moiety selected from $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$, 2,2'-ethylenedioxydiethylamine, triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

$r = 0$ to 300 ;

the moiety is derivatized with branching groups; ~~wherein~~

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule; and, ~~wherein~~

the valency platform molecule has a single line of symmetry; ~~and wherein~~

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules; and

(b) a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites.

Claim 23 (withdrawn): The composition of claim 22, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 24 (cancelled)

Claim 25 (cancelled)

Claim 26 (withdrawn): The composition of claim 22, wherein the biologically active molecules comprise a polynucleotide.

Claim 27-31 (cancelled)

Claim 32 (withdrawn): The composition of claim 22 or 64, wherein the biologically active molecule is selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, and drugs.

Claim 33-34 (cancelled)

Claim 35 (withdrawn): The composition of claim 22, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 36 (withdrawn): The composition of claim 35 or 77, wherein the composition is suitable for the suppression of antibody production.

Claim 37 (cancelled)

Claim 38 (withdrawn): The composition of claim 35 or 77, wherein the composition is suitable for the treatment of human systemic lupus erythematosus.

Claim 39-42 (cancelled)

Claim 43 (withdrawn): The composition of claim 22, wherein the valency platform molecule comprises triethylene glycol.

Claim 44 (cancelled)

Claim 45 (withdrawn-currently amended): A method of making the composition of claim 22 or 64, wherein the biologically active molecule is a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least about 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded [[DNA]] polynucleotides.

Claim 46 (withdrawn): The composition of claim 22, wherein the conjugate comprises triethyleneglycol.

Claim 47-50 (cancelled)

Claim 51 (withdrawn): The composition of claim 35 or 77, wherein the composition is suitable for reducing antibody levels.

Claim 52 (withdrawn): The composition of claim 35 or 77 wherein at least one molecule of the biologically active molecules is an analog of an immunogen that binds specifically to an antibody to which the immunogen binds specifically and lacks T cell epitopes.

Claim 53 (withdrawn): The composition of claim 22 or 64, wherein the composition is suitable for reducing antibody levels.

Claim 54 (withdrawn): The composition of claim 22, wherein the conjugate comprises linking moieties bound to the valency platform molecule and to the biologically active molecules.

Claim 55-63 (cancelled)

Claim 64 (currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of ~~comprises~~:

(a) [[a]] an ethyleneoxide containing chemically defined valency platform molecule comprising a moiety selected from -CH₂(CH₂OCH₂)_iCH₂-, 2,2'-ethylenedioxydiethylamine,

triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

$r = 0$ to 300;

the moiety is derivatized with branching groups; ~~wherein~~

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule; and ~~wherein~~

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules ~~and wherein the valency platform molecule further comprises a moiety of the formula $\text{OCH}_2\text{CH}_2\text{O}$;~~ and

(b) a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites.

Claim 65 (withdrawn): The composition of claim 64, wherein the valency platform molecule has a single line of symmetry.

Claim 66 (previously presented): The composition of claim 64, wherein the biologically active molecules are the same.

Claim 67 (currently amended): The composition of claim 64 or 66, wherein said conjugate comprises two branching groups, providing a total of four attachment sites for the biologically active molecules.

Claim 68 (currently amended): The composition of claim 64 or 66, wherein the biologically active molecules comprise a polynucleotide.

Claim 69 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex.

Claim 70 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex of about 20 to about 50 base pairs in length.

Claim 71 (previously presented): The composition of claim 68, wherein the polynucleotide is synthetic.

Claim 72 (previously presented): The composition of claim 68, wherein the polynucleotide is prepared by molecular cloning.

Claim 73 (previously presented): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex having a B DNA type helical structure.

Claim 74 (previously presented): The composition of claim 64, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 75 (currently amended): The composition of claim 64, wherein the biologically active molecules are [[is]] selected from the group consisting of analogs of immunogens, haptens, mimotopes, and aptamers.

Claim 76 (previously presented): The composition of claim 64, wherein the chemically defined valency platform molecule is substantially nonimmunogenic.

Claim 77 (currently amended): The composition of claim 64 or 74, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 78 (cancelled)

Claim 79 (previously presented): The composition of claim 77, wherein the composition is suitable for injection.

Claim 80 (currently amended): The composition of claim 64 or 74, wherein the valency platform molecule comprises polyethylene glycol having a molecular weight of about 200 to about 8,000.

Claim 81 (withdrawn): The composition of claim 65, wherein the conjugate comprises a moiety having the formula $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$, wherein $r = 1$ to 300.

Claim 82 (withdrawn): The composition of claim 65, wherein the valency platform molecule comprises a moiety having the formula $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$, wherein $r = 1$ to 300.

Claim 83 (cancelled)

Claim 84 (currently amended): The composition of claim 64 or 74, wherein the valency platform molecule comprises triethylene glycol.

Claim 85 (cancelled)

Claim 86 (previously presented): The composition of claim 64, wherein the valency platform molecules have substantially homogeneous molecular weight.

Claim 87 (cancelled)

Claim 88 (cancelled)

Claim 89 (currently amended): The composition of claim 64[], or 74, wherein the conjugate comprises linking groups ~~bound to~~ that bind the valency platform molecule ~~and~~ to the biologically active molecules.

Claims 90-98 (cancelled)

Claim 99 (new): The conjugate according to claim 89, wherein the linking group is selected from the group consisting of a thio-6 carbon chain phosphate and a thio-6 carbon chain phosphorothioate.

Claim 100 (new): The conjugate of claim 89, wherein the linking group comprises an alkylsulfhydryl moiety and the attachment sites comprise thiophilic groups.

Claim 101 (new): The conjugate of claim 64 or 74, wherein the attachment sites are thiophilic groups.

Claim 102 (new): The conjugate of claim 101, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulfhydryl, and α,β -unsaturated sulfone.

Claim 103 (new): The conjugate of claim 101 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 104 (new): The conjugate of claim 103, wherein the attachment sites are α -haloacetyl groups.

Claim 105 (new): The conjugate of claim 104, wherein the α -haloacetyl is bromoacetyl.

Claim 106 (new): A conjugate formable by the conjugation of:

(a) an ethyleneoxide containing chemically defined valency platform molecule, wherein:

the valency platform molecule comprises branching groups that are derived from a diamino acid, triamine or amino diacid;

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule; and

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites; and

(b) a multiplicity of polynucleotides.

Claim 107 (new): The conjugate of claim 106, wherein the polynucleotides comprise a polynucleotide duplex.

Claim 108 (new): The conjugate of claim 106 or 107, wherein each of the polynucleotides comprises at least about 20 nucleotides.

Claim 109 (new): The conjugate of claim 106, wherein each of said polynucleotides comprises a single stranded polynucleotide consisting of approximately 20 alternating cytosine (C) and adenosine (A) nucleotides.

Claim 110 (new): The conjugate of claim 109, wherein a second single stranded polynucleotide consisting of approximately 20 alternating thymidine (T) and guanosine (G) nucleotides is annealed to each of said single stranded polynucleotides that consists of approximately 20 alternating cytosine (C) and adenosine (A) nucleotides to form a double-stranded polynucleotide conjugate.

Claim 111 (new): The conjugate of claim 107, wherein said polynucleotides individually comprise the polynucleotide duplex of the formula:



Claim 112 (new): A composition comprising the conjugate of claim 106 or claim 107, wherein the composition is suitable for reducing antibody levels.

Claim 113 (new): The conjugate of claim 106 or 110, wherein said polynucleotides are individually bound to the valency platform molecule via the 5' end of the polynucleotides.

Claim 114 (new): The conjugate of claim 106, 110 or 111, wherein the polynucleotides are individually bound to the valency platform molecule via linker molecules.

Claim 115 (new): The conjugate of claim 114 wherein each of the linker molecules is selected from a thio-6 carbon chain phosphate or a thio-6 carbon chain phosphorothioate.

Claim 116 (new): The conjugate of claim 114, wherein the linker molecules are each an alkylamino or alkylsulfhydryl moiety.

Claim 117 (new): The conjugate of claim 116, wherein the linker molecules are each an alkylsulfhydryl moiety.

Claim 118 (new): The conjugate of claim 116, wherein the alkylamino or alkylsulfhydryl moiety is introduced to the polynucleotide by phosphoramidite chemistry.

Claim 119 (new): The conjugate of claim 106, 110 or 111, wherein the attachment sites are thiophilic groups.

Claim 120 (new): The conjugate of claim 119, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulfhydryl, and α,β -unsaturated sulfone.

Claim 121 (new): The conjugate of claim 119 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 122 (new): The conjugate of claim 119, wherein the attachment sites are α -haloacetyl groups.

Claim 123 (new): The conjugate of claim 119, wherein the α -haloacetyl is bromoacetyl.

Claim 124 (new): A composition comprising the conjugate of claim 106, 110 or 111 in a pharmaceutically acceptable carrier.

Claim 125 (new): The conjugate of claim 106, 110 or 111, formulated with a pharmaceutically acceptable injectable vehicle.

Claim 126 (new): The composition of claim 64 or the conjugate of claim 106, 110 or 111, wherein the conjugate is a tolerogen.

Claim 127 (new): The composition of claim 112, wherein the composition is suitable for the treatment of human systemic lupus erythematosus.

Claim 128 (new): A method of making the conjugate of claim 107, the method comprising:

reacting (a) a multiplicity of single-stranded polynucleotides, each of which is at least about 20 nucleotides in length and has a functional group at or proximate one of its termini which is optionally derivatized with a linker group, with (b) attachment sites on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotide conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 129 (new): A method of making the composition of claim 64 or 106, the method comprising forming said conjugates by covalently bonding the biologically active molecules to the chemically-defined valency platform molecule to form a conjugate.

Claim 130 (new): The composition of claim 64 or 74, wherein the valency platform molecule comprises 2,2'-ethylenedioxydiethylamine.

Claim 131 (new): The composition of claim 64 or 74, wherein the valency platform molecule comprises $-\text{CH}_2(\text{CH}_2\text{OCH}_2)_r\text{CH}_2-$.

Claim 132 (new): The composition of claim 80, wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claim 133 (new): The composition of claim 84 wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.